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PATENT SPECIFICATION (11) 1 571 434

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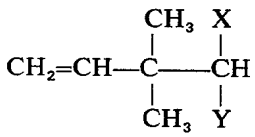
(54) NOVEL UNSATURATED DICARBOXYLIC ACID DERIVATIVES

(71) We, BAYER AKTIENGESELLSCHAFT, a body corporate, organised under the laws of Germany, of Leverkusen, Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

The present invention relates to certain unsaturated dicarboxylic acid derivatives and to a process for their preparation.

In particular, the present invention provides, as new compounds, the 1,1 - dimethyl - 2 - propenyl - malonic acid derivatives of the general formula



(IV),

in which

X and Y, which may be identical or different, each represent CN, the radical —COOR or the radical —COR¹, provided that X and Y do not both represent CN,

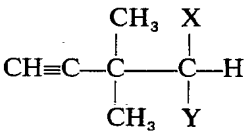
R represents C_1—C_4 alkyl, aralkyl or aryl, and R¹ represents C_1—C_4 alkyl.

Preferred compounds of the formula (IV) are those in which X and Y are identical or different and represent CN, acetyl (—$COCH_3$) or the radical —COOR in which R represents C_{1-4}-alkyl, benzyl or phenyl.

Compounds in which X and Y represent an alkoxycarbonyl group —COOR, in which R represents methyl, ethyl or tert. - butyl, are particularly preferred.

The present invention also provides a process for the preparation of a compound of the formula (IV) which comprises

(a) hyrogenating a dimethylpropynyl - malonic acid derivative of the general formula

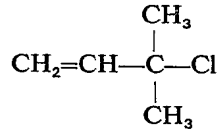


(V),

in which

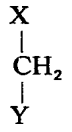
X and Y have the above-mentioned meanings, in the presence of a Lindlar catalyst, or

(b) reacting 3 - methyl - 3 - chloro - but - 1 - ene of the formula



(VI)

with a compound of the general formula



(VII)

in which

X and Y have the above-mentioned meanings,

in the presence of a basic catalyst and/or diluent (which term includes a solvent).

3 - Methyl - 3 - chloro - but - 1 - ene is known (see J. Chem. Soc. London 1948, page 530).

The compounds of the formula (VII) are known or can be prepared analogously to known processes.

The compounds of the formula (V) are known or can be prepared analogously to known processes (see J. Biol. Chem., volume 175, page 771; 1948).

The compounds of the formula (IV) are obtained from the starting materials of the

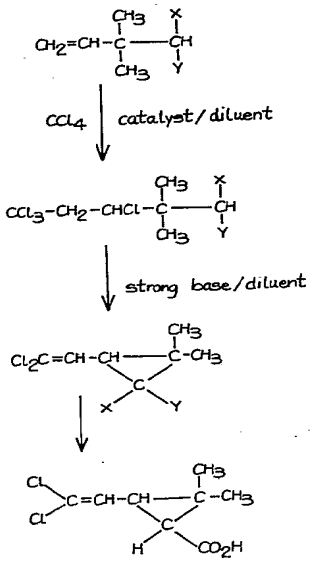
formula (V) by a reaction which is in itself known, that is to say the partial reduction of alkynes with hydrogen in the presence of so-called Lindlar catalysts, or by reacting 3 - methyl - 3 - chloro - but - 1 - ene with compounds of the formula (VII) in the presence of basic agents.

Basic agents which can be used are, for example, alkali metal hydroxides, such as NaOH or KOH, carbonates such as Na_2CO_3 or K_2CO_3, or, preferably, alcoholates, such as sodium methylate, sodium ethylate, sodium isopropylate or potassium tert.-butylate. In the latter case, the solvents used are preferably alcohols, such as methanol, ethanol, isopropanol or butanol.

Other solvents which can be used are: hydrocarbons, such as pentane, hexane or toluene, ethers, such as tetra - hydrofuran, dioxan, diisopropyl ether or glycol dimethyl ether, or ketones, such as acetone or butanone.

The reaction is carried out at temperatures between 0° and 150°C, e.g. between 0° and 100°C, and preferably between 20° and 100°C.

The compounds of the formula (IV) may be employed in the preparation of 2,2 - dimethyl - 3 - (2',2' - dichlorovinyl) - cyclopropane - 1 - carboxylic acid, according to the following reaction sequence:



The compounds of the formula (III) and their preparation by reacting compounds of the formula (IV) with carbon tetrachloride are the subject of copending U.K. Patent Application No. 39954/77 (Serial No. 1571433).

The conversion of the compounds (II) into the compound (I) is effected, depending upon the particular meanings of X and Y, by (a) complete or partial saponification and subsequent decarboxylation (b) elimination of an alkyl - carbonyl (—COR^1) group and saponification or (c) elimination of an acetyl radical and oxidation of the resulting ketone.

The compounds of the formula (II), their preparation and their conversion, by the above methods, into 2,2 - dimethyl - 3 - (2',2' - dichlorovinyl) - cyclopropane - 1 - carboxylic acid are disclosed and claimed in copending U.K. Patent Application No. 6465/77 (Serial No. 1571432).

The process of the present invention and methods of preparing appropriate starting materials are illustrated by the following Examples:

Example 1

113 g of dimethylpropynyl - malonic acid diethyl ester were dissolved in 500 ml of petroleum ether in a hydrogenation autoclave with a glass insert, 10 g of a Lindlar catalyst (5% Pd on $CaCO_3$) were added and the hydrogenation was carred out at 70°C until the theoretically calculated amount of hydrogen had been taken up. The mixture was then allowed to cool, the catalyst was filtered off and the solvent was stripped off under reduced pressure. 108 g of a very slightly yellowish coloured liquid remained and according to analysis by gas chromatography this consisted to the extent of 90% of 1,1 - dimethyl - 2 - propenylmalonic acid diethyl ester. Yield: 86% of theory. The nuclear magnetic resonance spectrum confirmed the structure: δ (in $CDCl_3$): 1.2 ppm (singlet+triplet, 12 protons); 3.3 ppm (singlet 1 proton); 4.15 ppm (quartet, 4 protons); 4.95 ppm and 6 ppm (multiplet; 2+1 protons).

Example 2

23 g of sodium were dissolved in 500 ml of absolute ethanol, 176 g of malonic acid diethyl ester were added dropwise, 1 g of hydroquinone was added and 104.5 g of 3 - chloro - 3 - methyl - 1 - butene (prepared according to J. Chem. Soc. London, *1948*, page 530) were then added dropwise at 60—70°C. When the dropwise addition was complete, the mixture was heated to the reflux temperature for a further one hour. It was then allowed to cool and left to stand overnight. After filtering, the sodium chloride which had been filtered off was rinsed with ethanol and the combined filtrates were concentrated *in vacuo*. The residue was rendered acid with ice-cold dilute hydrochloric acid and extracted three times with methylene chloride. The methylene chloride extracts were washed with sodium carbonate solution and then

with water, the organic phase was dried over sodium sulphate, the mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was subjected to fractional distillation. 161 g of a liquid which had a boiling point of 76—82°C/0.2 mm Hg were obtained. As was found by analysis by gas chromatography, the product was identical with the 1,1 - dimethyl - 2 - propenyl - malonic acid diethyl ester obtained in Example 1.

Example 3

23 g of sodium were dissolved in 500 ml of absolute ethanol, 124 g of cyanoacetic acid ethyl ester were added dropwise and 102.5 g of 3 - chloro - 3 - methyl - 1 - butyne (prepared according to J. Am. Chem. Soc. 79, 2,142; 1957) were then added dropwise at 60—70°C. When the dropwise addition was complete, the mixture was heated to the reflux temperature for a further one hour. After cooling, it was evaporated in a rotary evaporator and the residue was rendered acid with ice-cold dilute hydrochloric acid and extracted three times with methylene chloride. The methylene chloride extracts were washed with sodium carbonate solution and then with water and the organic phase was dried over sodium sulphate, filtered and concentrated under reduced pressure. The residue was subjected to fractional distillation under a high vacuum. 1,1 - Dimethyl - 2 - propynyl - cyanoacetic acid ethyl ester boiled at a boiling point of 92—98°C/0.5 mm Hg. The nuclear magnetic resonance spectrum confirmed the structure:

δ (in $CDCl_3$): 1.3 ppm (triplet, 3 protons); 1.5 ppm (singlet, 6 protons); 2.4 ppm (singlet, 1 proton); 3.6 ppm (singlet, 1 proton) and 4.3 ppm (quartet, 2 protons).

Example 4

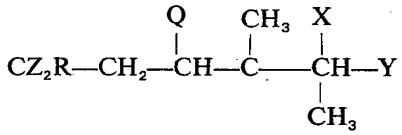
89.5 g of 1,1 - dimethyl - 2 - propynyl - cyanoacetic acid ethyl ester were dissolved in 500 ml of petroleum ether in a hydrogenation autoclave with a glass insert, 10 g of Lindlar catalyst (5% Pd on $CaCO_3$) were added and the hydrogenation was carried out at 60—80°C until the theoretically calculated amount of hydrogen had been taken up. After cooling, the catalyst was filtered off and the solvent was removed under reduced pressure. 81 g of a yellow oil which consisted mainly of 1,1 - dimethyl - 2 - propenyl - cyanoacetic acid ethyl ester remained.

Example 5

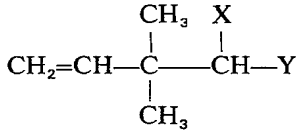
23 g of sodium were dissolved in 500 ml of absolute ethanol, 174 g of acetoacetic acid tert. - butyl ester were added, 1 g of hydroquinone was added and 104.5 g of 3 - chloro - 3 - methyl - 1 - butene were then added dropwise at 60°C. When the dropwise addition was complete, the mixture was heated to the reflux temperature for a further one hour. It was then allowed to cool and left to stand overnight. The sodium chloride which had precipitated was filtered off and washed with ethanol and the solvent was stripped off from the combined filtrates under reduced pressure. The residue was rendered neutral with ice-cold dilute hydrochloric acid and extracted three times with methylene chloride. The methylene chloride extracts were dried over sodium sulphate, the sodium sulphate was filtered off and the filtrate was concentrated *in vacuo*. The residue was subjected to fractional distillation under a high vacuum. 1,1 - Dimethyl - 2 - propenyl - acetoacetic acid tert. - butyl ester boiled at a boiling point of 62—66°C/0.08 mm Hg. The nuclear magnetic resonance spectrum confirmed the structure:

δ (in $CDCl_3$): 1.05 ppm (singlet, 9 protons); 1.3 ppm (singlet, 6 protons); 2.2 ppm (singlet, 3 protons); 3.5 ppm (singlet, 1 proton) and 4.9 and 5.9 ppm (multiplet, 2+1=3 protons).

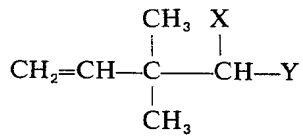
We are aware of the complete specification of Patent No. 1 520 024 which describes and claims, inter alia, a process for preparing a compound of the formula



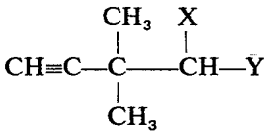
wherein X and Y are independently selected from cyano and alkoxycarbonyl containing from 1 to 4 carbon atoms in the alkoxy group, and Q, R and Z are independently selected from chlorine and bromine, provided that Q is always bromine, when either of Z and R is bromine, which process comprises reacting a compound of formula:



with a tetrahalomethane of formula CZ_2QR where Q and R are independently selected from chlorine and bromine provided that Q is always bromine when either of Z and R is bromine, in the presence of a free radical catalyst, and wherein as a preliminary step the compound of formula:



is obtained by hydrogenation under pressure of a compound of formula:



in the presence of a partially poisoned palladium catalyst.

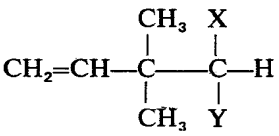
In such a process the palladium catalyst may be palladium on charcoal and the hydrogenation may be carried out in the presence of quinoline.

It is to be understood that we make no claim to a process as claimed in the complete specification of Patent No. 1 520 024 as defined above.

Subject to the foregoing disclaimer

WHAT WE CLAIM IS:—

1. The compound of the general formula



(IV),

in which

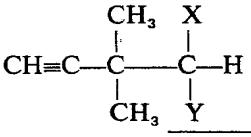
X and Y, which may be identical or different, each represent CN, the radical —COOR or the radical —COR^1, provided that X and Y do not both represent CN,

R represents C_1—C_4 alkyl, aralkyl or aryl, and R^1 represents C_1—C_4 alkyl.

2. Compounds according to claim 1, in which X and Y each represent CN, —$COCH_3$ or a radical —COOR wherein R represents C_1—C_4 alkyl, benzyl or phenyl.

3. Compounds according to claim 2, in which X and Y each represent a radical —COOR wherein R represents methyl, ethyl or tert. - butyl.

4. A process for the preparation of a compound according to claim 1 in which (a) a compound of the general formula

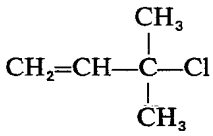


(V),

in which

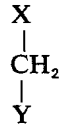
X and Y have the meanings stated in claim 1, is hydrogenated in the presence of a Lindlar catalyst, or

(b) 3 - methyl - 3 - chloro - but - 1 - ene, of the formula



(VI)

is reacted with a compound of the general formula



(VII)

in which

X and Y have the meanings stated in claim 1, in the presence of a basic catalyst and/or a diluent.

5. A process according to claim 4(b), in which the basic agent is an alkali metal hydroxide, an alkali metal carbonate or an alkali metal alcoholate.

6. A process according to claim 5, in which an alkali metal alcoholate is employed in the presence, as a solvent, of an alcohol.

7. A process according to claim 4(b), 5 or 6, in which the reaction is effected at between 0° and 150°C.

8. A process according to claim 7, in which the reaction is effected at between 0° and 100°C.

9. A process for the preparation of a compound according to claim 1, substantially as described in Example 1, 2, 4 or 5.

10. Compounds according to claim 1, whenever prepared by a process according to any one of claims 4 to 9.

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